UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

JANINE ALI, Plaintiff, v. ELI LILLY AND COMPANY, an Indiana corporation, Defendant.	Case No. 1:14-cv-01615-AJT-JFA Hon. Anthony J. Trenga Hon. John F. Anderson **MEMORANDUM IN SUPPORT OF PLAINTIFF'S MOTION TO COMPEL TWO FED. R. CIV. P. 30(b)(6) DEPOSITIONS AND THE DEPOSITION OF TORKIL FREDBORG**
GILDA HAGAN-BROWN, Plaintiff, v. ELI LILLY AND COMPANY, an Indiana corporation, Defendant.	Case No. 1:14cv-01614-AJT-JFA Hon. Anthony J. Trenga Hon. John F. Anderson **MEMORANDUM IN SUPPORT OF PLAINTIFF'S MOTION TO COMPEL TWO FED. R. CIV. P. 30(B)(6) DEPOSITIONS AND THE DEPOSITION OF TORKIL FREDBORG**

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INTRODUCTION

This motion, brought pursuant to Fed. R. Civ. P. 37(a), seeks an order compelling Defendant Eli Lilly and Company ("Lilly") to designate a Rule 30(b)(6) witness for deposition on two topics and produce Torkil Fredborg for deposition.

Lilly refuses to produce a Rule 30(b)(6) witness to testify about the development and creation of the European label for Cymbalta. Even though Lilly has already admitted the information on the European label is accurate and correct, Lilly maintains that any discovery concerning a foreign label is irrelevant and not discoverable. Lilly has drawn a bright-line and refuses to produce a corporate representative. This refusal is improper. As discussed below and in prior briefing, the content of the European label with regard to the withdrawal warning is markedly different than the U.S. label. CITE. Instead of the euphemistic "greater than 1%" warning that is used on the U.S. Label, the European label provides a clear warning of 45% and other information about the severity and duration of potential withdrawal, and directions for tapering. Plaintiffs should be allowed to conduct discovery about what Lilly understood and appreciated about the withdrawal warnings on the Cymbalta label as it existed in Europe. Such information goes directly to knowledge and intent and is reasonably calculated to lead to relevant information.

Lilly also refuses to produce a Rule 30(b)(6) witness to testify about the development and creation of the Cymbalta capsule and doses. According to Lilly, any claims alleging a design or labeling defect is preempted by federal law. This, however, is not a proper ground to refuse discovery. Preemption is an affirmative defense and a defendant cannot simply refuse to respond to discovery because it believes it will prevail on an affirmative defense. Otherwise, no discovery would ever occur. Plaintiffs have a right to question Lilly about what it knows and

understands about the Cymbalta capsule as that information goes to the heart of this litigation. More importantly, to the extent that Lilly believes this case is preempted, even a cursory reading of the seminal decision of *Wyeth v. Levine*, 555 U.S. 555 (2009) indicates it is not. As a brand manufacturer of a drug, Lilly bears responsibility for Cymbalta and federal law allows for the enforcement of state law actions. *See, e.g.*, *Saavedra v. Eli Lily & Co.*, No. 2:12-CV-9366-SVW-MAN, 2013 WL 6345442, at *7 (C.D. Cal. Feb. 26, 2013) (rejecting preemption claims in Cymbalta withdrawal litigation).

Finally, Lilly also refuses to produce Torkil Fredborg for a deposition. As discussed below, Mr. Fredborg played a key role in the drafting and development of the withdrawal warning in the European label and, as shown in numerous emails below, played a central role in monitoring the safety profile of Cymbalta globally. Lilly refuses to produce Mr. Fredborg for a deposition because Lilly believes his testimony would only be material to European labeling matters, which are, according to Lilly, not-discoverable. Again, this is not correct. And, in any event, Mr. Fredborg's experience with Cymbalta was never limited to just European matters. He worked on global safety. Therefore, even if this Court were to hold that European regulatory material is non-discoverable, Mr. Fredborg's testimony would still be relevant to show Lilly's knowledge and appreciation of the Cymbalta withdrawal risk profile.

BACKGROUND

On March 23, 2015, Plaintiffs Ali and/or Hagan-Brown served a deposition notice pursuant to Fed. R. Civ. P. 30(b)(6), designating four topics: (1) Cymbalta clinical trials, (2) the development and creation of the European Cymbalta label, (3) Lilly's marketing relationship with WebMD, and (4) the development and creation of the Cymbalta capsule and dosing levels.[1]

[1] A more exacting description of the 30(b)(6) categories is provided in the Argument section.

(*See* 30(b)(6) Deposition Notice at 2-6, Exh. X to Wisner Decl.) Lilly agrees to produce a Rule 30(b)(6) witness on the topic of Cymbalta's clinical trials (Madelaine M. Wohlreich), but objects to any depositions related to the remaining three topics. The parties met and conferred on Friday, April 3, 2015 following the last hearing, and exchanged several emails on this issue. Exhibit XXX at X. Despite a good faith effort to resolve this discovery dispute, the parties could not come to an agreement on whether Lilly would produce a Rule 30(b)(6) witness on the second and fourth topics, i.e., the development and creation of the European Cymbalta label and the development and creation of the Cymbalta capsule and doses.

In addition to the Rule 30(b)(6) deposition notice, on March 23, 2015, Plaintiffs served deposition notices for eight Lilly employees, one of which is Torkil Fredborg. Mr. Fredborg is a current Lilly employee based in the United Kingdom. As discussed below, Mr. Fredborg played a significant role in developing the European label for Cymbalta and was a key member of Lilly's regulatory and medical team tasked with monitoring Cymbalta's safety profile. Lilly has produced part of Mr. Fredborg's emails as they exist on Lilly's U.S. email servers, and is in the process of producing Mr. Fredborg's remaining emails from Lilly's European servers. Lilly, however, has objected to any deposition of Mr. Fredborg. Despite a good faith effort to resolve this issue, the parties could not reach an agreement. *See* Exhibit XXX at X (emails between counsel discussing the propriety of Mr. Fredborg's deposition).

LEGAL STANDARD

Discovery "is broad in scope and freely permitted." *Carefirst of Md., Inc. v. Carefirst Pregnancy Centers, Inc.,* 334 F.3d 390, 402 (4th Cir. 2003). "In essence, a party is entitled to any nonprivileged information that is relevant to a claim or defense in the matter." *Humanscale Corp. v. CompX Int'l, Inc.*, No. 3:09-CV-86, 2009 WL 5091648, at *1 (E.D. Va. Dec. 24, 2009)

(citing Fed. R. Civ. P. 26(b)). Relevant information need not be admissible at trial, it simply must appear "reasonably calculated to lead to the discovery of admissible evidence." Fed. R. Civ. P. 26(b)(1); *Wu v. Tseng*, 2007 WL 4143077, at *3 (E.D. Va. 2007). "[T]he burden of proof is with the party objecting to the discovery to establish that the challenged production should not be permitted." *Singletary v. Sterling Transp. Co.*, 289 F.R.D. 237, 241 (E.D. Va. 2012).

ARGUMENT

There are, at base, three issues that are the subject of this motion to compel:

(I) Whether Lilly should produce a Rule 30(b)(6) witness to offer testimony about the development and creation of the European Cymbalta label;

(II) Whether Lilly should produce a Rule 30(b)(6) witness to offer testimony about the development and creation of the Cymbalta capsule and doses; and

(III) Whether Lilly should produce Torkil Fredborg for deposition.

Each of these topics is addressed in turn.

I. Rule 30(b)(6) Testimony about the Creation and Development of the European Cymbalta Label Is Relevant Because it Shows Lilly's Knowledge and Understanding of the Cymbalta Withdrawal Risk and Whether the Equivalent U.S. Label Adequately Warned about the Frequency, Severity, and Duration of Cymbalta Withdrawal

One of the central allegations in this lawsuit is that the U.S. Cymbalta label fails to adequately warn patients and doctors about the frequency, severity, and duration of Cymbalta withdrawal. With regard to Cymbalta withdrawal, the U.S. label states:

> Discontinuation symptoms have been systematically evaluated in patients taking duloxetine [Cymbalta]. Following abrupt or tapered discontinuation in placebo-controlled clinical trials, the following symptoms occurred at a 1% or greater and at a significantly higher rate in duloxetine-treated patients compared to those discontinuing from placebo: dizziness, nausea, headache, paresthesia, fatigue, vomiting, irritability, insomnia, diarrhea, anxiety, and hyperhidrosis.
>
> During marketing of other SSRIs and SNRIs (serotonin and norepinephrine reuptake inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including

> the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. Although these events are generally self-limiting, some have been reported to be severe.
>
> Patients should be monitored for these symptoms when discontinuing treatment with Cymbalta. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment. then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate[.]

Exhibit 50 at 7 (CYM-00028684). The equivalent European label, however, contains the following warning:

> Withdrawal symptoms when treatment is discontinued are common, particularly if discontinuation is abrupt (see section 4.8). In clinical trials adverse events seen on abrupt treatment discontinuation occurred in approximately 45% of patients treated with Cymbalta and 23% of patients taking placebo. The risk of withdrawal symptoms seen with SSRI's and SNRI's may be dependent on several factors including the duration and dose of therapy and the rate of dose reduction. The most commonly reported reactions are listed in section 4.8. Generally these symptoms are mild to moderate, however, in some patients they may be severe in intensity. They usually occur within the first few days of discontinuing treatment, but there have been very rare reports of such symptoms in patients who have inadvertently missed a dose. Generally these symptoms are self-limiting and usually resolve within 2 weeks, though in some individuals they may be prolonged (2-3 months or more). It is therefore advised that duloxetine should be gradually tapered when discontinuing treatment over a period of no less than 2 weeks, according to the patient's needs (see section 4.2).

Exhibit 51 at 6. As discussed in prior briefing, and as outlined in Exhibit 52, there are important differences between the U.S. Cymbalta label and the European label. The European label contains significantly more information about the frequency, duration, and severity of withdrawal reactions. *See* Exhibit 52 at 1-3.

It has already been conclusively established "that the information contained in the European Medicines Agency Summary of Product Information for CYMBALTA is accurate and true." Exhibit 49 at 20, RFA no. 44; *see* Fed. R. Civ. P. 36(b) ("A matter admitted under this

rule is conclusively established[.]"). Thus, the statements made in the European label are admissions about which the Plaintiffs have a right to question Lilly. This is done through a Rule 30(b)(6) deposition. And here, the Rule 30(b)(6) deposition notice clearly outlined the specific issues Plaintiffs wish to discuss with an appropriate Lilly representative:

European Labeling for Cymbalta

1. The creation, development, writing, and approval of the European Medicines Agency Summary of Product Information for Cymbalta. For clarity, the witness should be able to testify with regard to the following:

   a. Why the rate of patients experiencing at least one DEAE reflected in the Perahia article was included in the European label.

   b. Why the words "withdrawal symptoms" were used in the European label rather than the words "discontinuation symptoms" in the U.S. Label.

   c. Why the duration of "withdrawal symptoms" in the European label is described differently from the duration of "discontinuation symptoms" described in the U.S. Label.

   d. Why the instruction "duloxetine should be gradually tapered when discontinuing treatment over a period of no less than 2 weeks" was included in the European label.

   e. Who and how Lilly communicated with the European Medicines Agency (or its predecessor, the European Agency for the Evaluation of Medicinal Products) pertaining to the European label.

   f. The process by which the Marketing Authorization Application (MAA), and any and all supplements thereto, was prepared and submitted by Lilly to the European Medicines Agency (or its predecessor, the European Agency for the Evaluation of Medicinal Products).

   g. The organization, structure, personnel, and document preparation and retention policies of Lilly's Global Product Labeling Committee (GPLC).

   h. The process by which all versions of the European SPC (Summary of Product Characteristics) was prepared and submitted by Lilly to the European Medicines Agency (or its predecessor, the European Agency for the Evaluation of Medicinal Products), and the custodian(s) thereof.

i. The process by which all versions of the RAPT (Regulatory Activity and Planning Tracker) was prepared and maintained by Lilly, and the custodian(s) thereof.

j. Who and how Lilly communicated with the CHMP (Committee for Medicinal Products for Human Use).

k. Who and how Lilly communicated with the European "Rapporteur", including (but not limited to) the 2005 Rapporteur assessment of Lilly's second periodic safety update report (PSUR).

Exhibit 1 at 4-5. On its face, these topics and issues are reasonably calculated to lead to discoverable information and, thus, Plaintiffs should be allowed to proceed with discovery. *See, e.g.*, *Hardy v. Pharmacia Corp.*, No. 4:09-CV-119 CDL, 2011 WL 2118983, at *3 (M.D. Ga. May 27, 2011) (allowing discovery about foreign labels because the information sought was reasonably calculated to lead to discoverable information); see also *Gen. Motors Corp. v. Lupica*, 237 Va. 516, 521, 379 S.E.2d 311, 314 (1989) ("[E]vidence is admissible in a products liability case to establish foreseeability . . . [w]hen a defendant has notice and actual knowledge of a defect, it owes a duty to a plaintiff 'to take the steps reasonably necessary to remedy the defect.'" (quoting *Gen. Motors Corp. v. Lupica*, 237 Va. 516, 521, 379 S.E.2d 311, 314 (1989)).

Here, Lilly argues that "[w]e will not produce a witness with respect to European labeling for Cymbalta. The European label has no bearing on your clients' claims." Exhibit 10 at 8 (citing *In re Seroquel Prods. Liab. Litig.*, No. 6:06-MD-1769-ORL-22-DAB, 2009 WL 223140, at *6 (M.D. Fla. Jan. 30, 2009), aff'd, 601 F. Supp. 2d 1313 (M.D. Fla. 2009); *In re Viagra Prods. Liab. Litig.*, 658 F. Supp. 2d 950, 965 (D. Minn. 2009). According to Lilly, foreign regulatory materials are not admissible in a products liability case. And, to be fair, there is some authority to support this argument. *See In re Viagra*, 658 F. Supp. 2d at 965 (holding foreign regulatory action irrelevant and inadmissible); *In re Seroquel Prods. Liab. Litig.*, 2009 WL

223140, at *6 (same). There is, however, significant authority holding the opposite as well. *In re Levaquin Products Liab. Litig.*, No. 08-1943 JRT, 2010 WL 4676973, at *4 (D. Minn. Nov. 9, 2010) (admitting foreign regulatory material); *Schedin v. Ortho-McNeil-Janssen Pharm., Inc.*, 808 F. Supp. 2d 1125, 1138 (D. Minn. 2011) (same) *aff'd in part, rev'd in part on other grounds In re Levaquin Products Liab. Litig.*, 700 F.3d 1161 (8th Cir. 2012); *In re Yasmin & YAZ (Drospirenone) Mktg., Sales Practices & Products Liab. Litig.*, No. 3:09-MD-02100-DRH, 2011 WL 6302287, at *27 (S.D. Ill. Dec. 16, 2011) (allowing expert to rely on foreign regulatory material to render opinions). As one federal court put it about another antidepressant's foreign labeling:

> This Court finds the foreign product labeling evidence relevant since it may potentially demonstrate the defendant's knowledge of potential side effects resulting from the ingestion of Paxil. The foreign labeling evidence may also demonstrate the adequacy of the warning provided by the defendant to customers in the United States. Further, this Court notes that the Food and Drug Administration regulates warnings which must be provided by pharmaceutical corporations. 21 C.F.R. § 201.57. However, said regulations regulate the type of information which must be included in the product information, the exact nature and language of such information is left to the manufacturer and distributor, it is not actually produced by the FDA. 21 C.F.R. § 201 .57. The defendant is free to present evidence to the jury regarding foreign "medical customs and practices that are different from those in the United States," but the Court does not find that such differences make the foreign labels irrelevant. Warning labels used in the United States and foreign countries all concern and relate to the defendant's SSRI, paroxetine, and are written and distributed by the defendant.

Estate of Tobin ex rel. Tobin v. Smithkline Beecham Pharm., No. CIV.00-CV-0025-BEA, 2001 WL 36102165, at *1 (D. Wyo. May 18, 2001); *see also Estates of Tobin by Tobin v. Smithkline Beecham Pharm.*, 164 F. Supp. 2d 1278, 1289 (D. Wyo. 2001).

Thankfully, this Court need not decide the ***admissibility*** of foreign labels at this time. That will be the topic of a motion *in limine* prior to trial. The issue here is ***discoverability***. And, discoverable information "need not be admissible at trial if discovery appears reasonably

calculated to lead to the discovery of admissible evidence." Fed. R. Civ. P. 26(b)(1); see *Hardy*, 2011 WL 2118983, at *3. As the *Hardy* court explained:

> Even if the foreign labels and product guides are not ultimately admissible at trial in this case, they could lead Plaintiff to discover admissible evidence regarding whether Defendants' warnings to Plaintiff's physician were adequate and reasonable under the circumstances. *Cf. Wyeth v. Levine,* 555 U.S. 555, 569 (2009) (noting that, after the first incident of severe complications similar to those experienced by the plaintiff, similar complications continued to occur, and the pharmaceutical company could have analyzed data regarding the similar complications and added a stronger warning regarding the drug). For example, Plaintiff could use the labels and product guides to discover *what Defendants knew about the potential risks* of the products at issue here, *when Defendants knew about those potential risks*, *what follow-up investigations Defendants did* to learn more about those potential risks, and other facts that are potentially relevant to the risk-utility analysis.

Id. (emphasis added). Here, allowing a deposition of a 30(b)(6) witness to answer questions about the European label is reasonably calculated to lead to discoverable information as it might reveal what Lilly "knew about the potential risks" or "when [Lilly] knew about those potential risks" or "what follow-up investigations" Lilly did (or did not do) to learn about the risk.

Moreover, there is significant evidence that there was cross-pollination between Lilly personnel in Europe and the U.S. on the withdrawal issue. For example, over a year before Cymbalta was approved in the U.S., a Lilly researcher based in the United Kingdom, Dr. David Perahia, expressed serious concerns about Lilly being forthright on the withdrawal issue:

> I must confess to being a little unco[m]fortable about the whole discontinuation thing. Maybe it's more of a **UK specific issue**, but ***paroxetine [Paxil] is taking a fearsome battering in the media over here*** at the moment, and a significant part of that is discontinuation-related stuff. ***It's clear that duloxetine has a significant DESS [discontinuation-emergent signs and symptoms] liability*** (on abrupt discontinuation, admittedly, but how much taper data do we have yet ?), and the perception will be further reinforced by our short [half-life] which is seen by many as being directly linked [redacted without explanation].[2]

[2] Dr. Michael Detke responded to this email, but that response is also redacted without any explanation. CITE. Plaintiffs have challenged the redactions on approximately 122 documents so far, including this one, and are awaiting Lilly's response.

> … If we're not careful, ***the environment is set for this to blow up in our faces*** unless we're proactive about it.

Exhibit 42 at 2 (CYM-01873415) (emphasis added). Dr. Perahia was given a glib response from a Madelaine Wohlreich (the subject of an upcoming deposition) and then stated:

> I sense we are being a bit complacent around this, and it could hurt us (e.g. no diffs from parox on abrupt discontinuation in our trials, short t1/2 etc. etc.)
>
> As an opening gambit, I would define proactive as:
>
> (1) Write up our data and get it published as a priority rather than dragging our heels
>
> (2) Consider running a trial which might add to the evidence base on how best to manage stopping the drug, e.g. over how long should drug be tapered? (open label treatment, then perhaps 3 arms looking at abrupt discontinuation vs. 2 week taper vs. 4 week taper in a double blind fashion, with frequent visits). ***Good PR due to being open and pushing the science***, ***with an evidence-based recommendation at the end to boot.***[3] I'm sure Matt[4] would blanch at this suggestion, ***but we can't just stick our head into the sand.***
>
> ***Paroxetine is being torn to pieces by the media (and in fact regulators too) over in Europe***, and much of the criticism is stemming from the perception that GSK have been, to put it politely, less than transparent about discontinuation with paroxetine and how best to manage it. I would rather we didn't fall into the same trap.

Exhibit 42 at 1 (CYM-01873414) (emphasis added).

This email demonstrates that there was no "Chinese wall" between Lilly's operations in Europe and Lilly's operations in the U.S. Dr. Perahia was actively warning Lilly executives about "stick[ing] [their] head into the sand" in the U.S., based on his perception of the regulatory climate *in Europe*. This is simply a reflection of the way Lilly's company was set up—there are countless examples of non-U.S. personnel interfacing with Lilly personnel in the U.S., discussing issues related to Cymbalta withdrawal. *See, e.g.*, Exhibit 11 at 1 (CYM-02821070) (email from

[3] There is no evidence that these studies were ever performed.

[4] Plaintiffs believe this is a reference to Matt Kuntz.

Mr. Torkil in the United Kingdom to Steve Sugino in Indianapolis discussing a potential 20 mg dose and its relationship to withdrawal); Exhibit 13 at 1-4 (CYM-01876671-74) (email from Dr. Crucitti in the United Kingdom to personnel, including Mary Nilsson, a statistician in the U.S., discussing whether there is a difference in withdrawal in abrupt or tapered discontinuation); Exhibit 15 at 1-4 (CYM-02367251-54) (email exchanges in which European Lilly personnel are reviewing adverse event protocol used in the U.S. relating specifically to withdrawal); *see* Exhibit 39 at 1-2 (CYM-01892231-32) (email discussions among personnel from U.K. and U.S. about withdrawal warnings for Cymbalta in Japan); Exhibit 26 at 1-2 (CYM-02238063-64) (U.S. Regulatory Scientist, Carol Stephens giving labeling advice for an appeal to an Australian regulatory agency).

It appears from the documents that the safety of Cymbalta was a global operation, with scientists from all over the world participating and discussing the safety issues with Cymbalta and how they apply to other countries *and* the U.S. *See, e.g.*, Exhibit 16 at 1-2 (CYM-02359370) (emails about how recent Cymbalta-warfarin interaction study had prompted label changes in Europe and how that affected U.S. labeling); Exhibit 19 at 1 (CYM-02328433) (email from U.S. medical advisor to U.K.-based Dr. Crucitti discussing withdrawal warnings in the U.S. label and core data sheet (CDS)); Exhibit 25 at 1-3 (CYM-02279719-21) (email exchanges wherein Lilly personnel in the U.S. are drafting withdrawal warning language for the European label); Exhibit 27 at 1 (CYM-02269272) (email from U.S. regulatory advisory giving updated information about U.S. label changes and updates to Mr. Fredborg). Lilly's attempt to carve out the "relevance" of the information that foreign regulatory personnel might possess is untenable. Plaintiffs should be allowed to conduct discovery about the European Cymbalta label. Plaintiffs request that the Court enter an order compelling Lilly to produce a properly designated Rule 30(b)(6) witness on

this topic.

II. Rule 30(b)(6) Testimony about the Development of the Cymbalta Capsule and Dosing Regimens Is Relevant Because It Goes to Lilly's Knowledge and Understanding of the Inability of Patients to Taper Below 20 Mg and the Risks of Withdrawal

Plaintiffs allege that one of the reasons Cymbalta is defectively designed and labeled is because the smallest dose available is 20 mg, which means any patient who wants to quit taking Cymbalta will have to stop abruptly taking 20 mgs at some point. This problem is compounded by the fact that the label states that "Cymbalta should be swallowed whole and should not be chewed or crushed, not should the capsule be opened and its contents sprinkled on food or mixed with liquids. All of these might affect the enteric coating." Exhibit 50 at 3 (CYM-00028680). Patients and doctors cannot create "smaller" tapering doses without potentially ruining the enteric coating for Cymbalta and rendering the medication unsafe. *See* Exhibit 53 at 1 (CYM-02053036) (memorandum from the FDA to Lilly in 2007 in which the FDA "identified a signal involving the opening of Cymbalta capsules prior to administration to achieve a lower dose of the drug."). Plaintiffs allege that Lilly should have designed the Cymbalta capsule to allow for smaller tapering doses, manufactured smaller tapering doses to allow patients to safely discontinue Cymbalta below 20 mg a day, or properly labeled this issue so that patients and physicians could know about this issue before taking the drug.

This theory of liability prompted Plaintiffs' 30(b)(6) deposition notice, which asked Lilly to produce a witness that could testify about:

> **The Cymbalta Capsule**
>
> 1. The design and dosing of the Cymbalta capsule. For clarity, the witness should be able to testify with regard to the following:
>
>   a. Why was a 20 mg dose of Cymbalta created[?] Who was responsible for making decisions about the available dosing levels for Cymbalta[?]

b. Why is the Cymbalta capsule in an enteric coating[?] Why was Cymbalta designed in a capsule form? How do the pellets within the Cymbalta capsule work in the absorption of the drug[?]

c. Why does the Cymbalta label advise against opening the Cymbalta capsule? What safety / efficacy concerns are associated with ingestion of Cymbalta outside of the capsule?

d. Were smaller doses, i.e., 10 or 5 mg ever considered? If so, why were they never created?

Exhibit 1 at 5-6. The purpose of this deposition is explore the creation and development of the Cymbalta capsule so as to determine whether Lilly acted negligently in selling a drug that was, by its design and labeling, unsafe with regard to withdrawal risks.

Lilly, however, "will not produce a witness regarding the Cymbalta capsule." Exhibit 10 at 8. Lilly did not expressly state why it would not produce such a witness but, instead, cited several cases involving federal preemption.[5] *Id.* Lilly apparently believes that any claim that the design and labeling of Cymbalta was defective is preempted by federal law. This argument, however, is misplaced.

First, federal preemption is an "an affirmative defense upon which the defendants bear the burden of proof[.]'" *Bruesewitz v. Wyeth LLC*, 131 S. Ct. 1068, 1087, n.2 (2011) (quoting *Fifth Third Bank ex rel. Trust Officer v. CSX Corp.*, 415 F.3d 741, 745 (7th Cir. 2005)). It is "a demanding defense" which begins with a strong presumption against preemption. *Wyeth v. Levine*, 555 U.S. 555, 565, 573 (2009). And, as an affirmative defense, it cannot be a valid ground for withholding discovery. Otherwise, Lilly would be permitted to withhold nearly all discovery, citing the forty-five defenses raised in its answer. The issue of preemption should not

[5] Lilly cites both *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2574, 180 L. Ed. 2d 580 (2011) and *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2475, 186 L. Ed. 2d 607 (2013) to support an inference that claims against Lilly related to its design and labeling of Cymbalta are preempted. These cases, however, are both solely concerned with whether state law claims against generic manufacturers—not brand name manufacturer—are preempted because generic manufacturers do not control the labeling. Attempting to apply *Mensing* and *Bartlett* to a brand manufacturer, which controls the content of the drug's label, is completely misplaced.

be raised in the context of a motion to compel, or even a discovery dispute—it should be noticed and briefed as a motion for summary judgment.

Second, any claim of preemption is meritless. *See, e.g.*, *Saavedra*, 2013 WL 6345442, at *7 (rejecting preemption claims in Cymbalta withdrawal litigation). There is significant evidence in the record that Lilly was made aware of the problem of tapering off Cymbalta after the drug was initially approved and, thus, could have taken action to comply with state law disclosure requirements. *See Levine*, 555 U.S. at 570-71 ("[I]t has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times. It is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market."). For example, in 2007, the FDA issued a memorandum to Lilly identifying "a signal involving the opening of Cymbalta capsules prior to administration to achieve a lower dose of the drug." Exhibit 53 at 1 (CYM-02053036). The memorandum provides explicit examples of cases involving "opening 20 mg capsules while tapering off of Cymbalta to avoid withdrawal effects" and that "An 18 year old woman was attempting taper off of Cymbalta after more than 15 months of receiving 60 mg daily. She was having withdrawal symptoms. . . [S]he decreased the dose by taking part of a 20 mg capsule." *Id.* at 3, 14 (CYM-02053038, 49). In 2008, Lilly was confronted by regulatory authorities in Europe, which demanded inclusion of language about use of 20 and 30 mg doses to help with withdrawal reactions. Exhibit 43 at 1 (CYM-01865817); Exhibit 11 at 1 (CYM-02821070). And, there are also numerous examples of Lilly reanalyzing withdrawal data and the effects of tapering versus abrupt discontinuation. *See* Exhibit 44 at 1 (CYM-01812103); Exhibit 48 at 1-5 (CYM-01780840-43); Exhibit 41 at 1 (CYM-01876671). Lilly had the ability to make changes to the label to properly warn about the issues associated with discontinuing from a 20 mg dose.

There is no valid claim for preemption.

Third, assuming *arguendo* that some portion of Plaintiffs' design defect claim were preempted by federal law, nothing would prevent the Plaintiffs from conducting discovery about what information Lilly possessed about the design and dosing of the Cymbalta capsule as that information would be material to a failure-to-warn claim, i.e., what information Lilly possessed about a safety defect.

As it stands, Lilly's refusal to provide a witness to testify about the design of the Cymbalta capsule and the decisions that went into creating Cymbalta's various doses is improper. Plaintiffs have served a valid Rule 30(b)(6) deposition notice on a topic that is clearly designed to lead to discoverable information. Plaintiffs request that the Court enter an order compelling Lilly to produce a properly designated Rule 30(b)(6) witness on this topic.

III. Torkil Fredborg Played a Key Role in Developing the Cymbalta Label In Europe and Maintaining the Safety Data on Lilly's Core Data Sheet and Plaintiffs Should Be Allowed to Take His Deposition

Torkil Fredborg is currently a regulatory advisor for Lilly based in the U.K. Plaintiffs would like to depose Mr. Fredborg to ask "about his understanding of the withdrawal risk of Cymbalta, his discussions with various Lilly personnel about that risk, i.e., Dr. Detke, Dr. Perahia, and Dr. Wohlreich, what information was exchanged about the reasons the European label would contain some accurate risk information and the U.S. label would not, etc." Exhibit 10 at 6. There is evidence that Mr. Fredborg has relevant information and testimony.

It appears that Mr. Fredborg played a key role in the development of the language in the European label dealing with withdrawal—the language that Lilly has admitted is true and correct. Based on an email, dated October 4, 2006, European regulatory authorities asked Lilly for "an analysis of the withdrawal symptoms reported on duloxetine discontinuation" as part of

"a reaction to [Lilly's] proposal that the symptoms in the requested class labeling statement have not been reported for duloxetine." Exhibit 45 at 2 (CYM-01799109); *see also* Exhibit 14 at 1 (CYM-02547795) (discussing whether the word "taper" should be added to the European label in response to information sent from a U.S. regulatory consultant). In the October 4, 2006 email, Mr. Fredborg is organizing a meeting to arrange for a "withdrawal symptom analysis." Exhibit 45 at 2 (CYM-01799109). Although much of the document is redacted for no apparent reason, the email indicates that Mr. Fredborg was instrumental in cultivating the language on the European label. *See also* Exhibit 25 at 1 (CYM-02279719) (emails sent to Mr. Fredborg about how the percentages for withdrawal reactions were calculated for inclusion in the European label).

It also appears that Mr. Fredborg was kept apprised of developments and changes that were occurring with the U.S. label. *E.g.*, Exhibit 27 at 1 (CYM-02269272) (""[J]ust to have 'in your back pocket' . . .this slide set summarizes all the recent and upcoming USPI [U.S. Product Insert] changes."); see Exhibit 12 at 1 (CYM-02739007) (Mr. Fredborg copied on email update about discontinuation warning for global core data sheet); Exhibit 17 at 1-3 (CYM-02337681-84) (Mr. Fredborg is included on communications about how a new study impacts U.S. labeling). And, in 2008, when Lilly elected to secure a 20 mg dose in Europe, Mr. Fredborg shared his thoughts about how the medically-ineffective dose would be perceived and shared the proposed labeling from European authorities with Lilly executives in the U.S. Exhibit 43 at 1 (CYM-01865817). He explained that "[w]hile we wanted to avoid the specific mentioning of 20mg in the SPC, I do believe that the proposed wording still offers flexibility to consider where to market the 20 mg dose." *Id.* Then a few months later, Mr. Fredborg discussed how Lilly could leverage the withdrawal issue to help obtain approval for a 20 mg dose:

> [S]ome patients might need a longer taper, and the only way that this can currently be done is via alternate day dosing. This practice carries the theoretical risk of itself inducing discontinuation symptoms in some patients due to the enforced interruption of treatment which is precisely what the taper should be designed to avoid. The availability of a 20 mg formulation would allow clinicians to reduce the dose of duloxetine more gradually at the end of treatment, where necessary - for example 60 mg to 40 mg to 30 mg to 20 mg to zero - without the need to resort to alternate day dosing.

Exhibit 11 at 1 (CYM-02821070).

Lilly refuses to produce Mr. Fredborg for deposition. Lilly believes that his testimony is irrelevant because he is based in Europe and works primarily on European regulatory matters. *See* Exhibit 10 at 2. Plaintiffs have already addressed this concern above—foreign regulatory matters are the proper subject of discovery. Moreover, as described in the above emails, there is evidence that Mr. Fredborg possesses knowledge about Cymbalta withdrawal beyond the limited purlieu of European regulatory matters. Plaintiffs request that the Court enter an order compelling Lilly to produce Mr. Fredborg for deposition.

CONCLUSION

For the forgoing reasons, Plaintiffs respectfully request that this Court enter an order compelling Lilly to provide Rule 30(b)(6) witnesses to testify about the development and creation of the European Cymbalta label and the design and dosing regimen for Cymbalta. Plaintiffs also respectfully request that the Court enter an order compelling Lilly to produce Torkil Fredborg to appear for deposition.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on the 10th day of April, 2015, a true copy of the foregoing MEMORANDUM IN SUPPORT OF PLAINTIFF'S MOTION TO COMPEL was filed electronically with the Clerk of Court using the CM/ECF system, which will send a notification of such filing to the following:

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